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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/942,174	08/29/2001	Ish Kumar Khanna	SO3285-US	6799

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HARNESS, DICKEY, & PIERCE, P.L.C
7700 BONHOMME, STE 400
ST. LOUIS, MO 63105

EXAMINER

COLEMAN, BRENDA LIBBY

ART UNIT PAPER NUMBER

1624

DATE MAILED: 08/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/942,174

Applicant(s)

KHANNA ET AL.

Examiner

Brenda Coleman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 May 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 8-11, 13 and 15 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 8-11, 13 and 15 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Claims 8-11, 13 and 15 are pending in the application.

This action is in response to applicant's amendment filed May 11, 2004. Claims 1-7, 12, 14 and 16 were canceled and claims 8, 9, 11 and 13 have been amended.

Response to Amendment

The applicant's amendments filed May 11, 2004 have been fully considered with the following effect:

1. With regards to the 35 U.S.C. § 112, first paragraph rejection of claims 10-16 of the last office action labeled paragraph 2, the applicant's arguments have been fully considered, however they were not found persuasive. The applicant's stated that claim 11 as amended provides a method for treating $\alpha_v\beta_3$ -mediated tumor metastasis, $\alpha_v\beta_3$ -mediated tumor growth and $\alpha_v\beta_3$ -mediated solid tumor growth rather than merely tumor metastasis, tumor growth and solid tumor growth generally. The applicants also stated that it is well known within the art of oncology that the $\alpha_v\beta_3$ integrin plays a role in various conditions or disease states including tumor metastasis, solid tumor growth (neoplasia), osteoporosis, Paget's disease, humoral hypercalcemia of malignancy, osteopenia, endometriosis, angiogenesis, including tumor angiogenesis, retinopathy including macular degeneration, arthritis, including rheumatoid arthritis, periodontal disease, psoriasis and smooth muscle cell migration (e.g. restenosis) and arteriosclerosis. However, recent journal article of Reynolds et al., herein provided indicates that $\alpha_v\beta_3$ and $\alpha_v\beta_5$ integrins are not essential for tumor angiogenesis. Reynolds reports that mice lacking β_3 integrins or both β_3 and β_5 integrins not only support tumorigenesis, but have enhanced tumor growth as well. The data of Reynolds

indicates that $\alpha_v\beta_3$ and $\alpha_v\beta_5$ integrins are not essential for vascular development or pathological angiogenesis and highlight the need for further evaluation of the mechanisms of action of α_v -integrin antagonists in anti-angiogenic therapeutics.

As stated in the MPEP, 2164.08 "[t]he Federal Circuit has repeatedly held that the specification must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557, 1561 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). Nevertheless, not everything necessary to practice the invention need be disclosed. In fact, what is well-known is best omitted. In re Buchner, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991). All that is necessary is that one skilled in the art be able to practice the claimed invention, given the level of knowledge and skill in the art. Further the scope of enablement must only bear a reasonable correlation to the scope of the claims. See, e.g., In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). As concerns the breadth of a claim relevant to enablement, the only relevant concern should be whether the scope of enablement provided to one skilled in the art by the disclosure is commensurate with the scope of protection sought by the claims. In re Moore, 439 F.2d 1232, 1236, 169 USPQ 236, 239 (CCPA 1971). See also Plant Genetic Sys., N.V. v. DeKalb Genetics Corp., 315 F.3d 1335, 1339, 65 USPQ2d 1452, 1455 (Fed. Cir. 2003) (alleged pioneer status of invention irrelevant to enablement determination)."

Claims 10, 11, 13 and 15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for reasons of record and stated above.

2. The applicants amendments and arguments are sufficient to overcome the 35 U.S.C. § 112, second paragraph rejections labeled d), f) and i) maintained in the last office action, which are hereby **withdrawn**. However, with regards to the 35 U.S.C. § 112, second paragraph rejection labeled g) and h), the applicant's amendments and remarks have been fully considered but they are not persuasive.

g) The applicants' stated that as described above with respect to the rejection under 35 U.S.C. § 112, first paragraph, Applicants respectfully submit that amended claims 10, 11, 13 and 15 are sufficiently clear such that one skilled in the art would be able to practice the present invention. However, this is not so as outlined above in the response to the applicants 35 U.S.C. § 112, first paragraph.

h) The applicant's stated that the term chemotherapeutic agent is sufficiently clear to be understood by one of ordinary skill in the art. If the scope of the subject matter embraced by the claims is clear, and if applicants have not otherwise indicated that they intend the invention to be of a scope different from that defined in the claims, then the claims comply with 35 U.S.C. § 112, second paragraph. However, the indefiniteness of this term is such that it is not known what chemotherapeutic agents are embraced by the term "chemotherapeutic agent".

Claims 10, 11, 13 and 15 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for reasons of record and stated above.

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3. The applicants' amendments and arguments are sufficient to overcome the 35 U.S.C. § 112, second paragraph rejections labeled a), c), d) and e) in the last office action, which are hereby **withdrawn**. However, with regards to the 35 U.S.C. § 112, second paragraph rejection labeled b), the applicant's amendments and remarks have been fully considered but they are not persuasive.

b) The applicants' stated that the depiction of Z^1 on the A-B ring has been amended to more clearly indicate that Z^1 is a divalent moiety and that the depiction includes Z^1 to show its position relative to the A-B ring; however, Z^1 remains bonded to Z^2 as shown in Formula I. The definition of ring A-B is such that the ring is $-Z^1-1-oxo-isoquinolin-2-yl-$. This is not a definition of $-Z^1-(ring\ A-B)-$ and hence the structure of formula I with ring A-B defined as $-Z^1-1-oxo-isoquinolin-2-yl-$ becomes, $A^1-Z^2-Z^1-Z^1-1-oxo-isoquinolin-2-yl-X-(CH_2)_nCOR^b$.

Claims 8, 10, 11, 13 and 15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for reasons of record and stated above.

4. With regards to the obviousness-type double patenting rejection of claims 8-16 of the last office action, the applicant's arguments have been fully considered, however they were not found persuasive. The applicants stated that no subject matter of either application has yet been found to be allowable and submit that this rejection is premature. However, as stated in the last office action is a **provisional** (because the

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conflicting claims have not in fact been patented) obviousness-type double patenting rejection between two applications.

Claims 8-11, 13 and 15 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 8-15 of copending Application No. 10/363,070, for reasons of record and stated above.

In view of the amendment dated May 11, 2004, the following new grounds of rejection and/or reinstated rejections apply.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 8, 10, 11, 13 and 15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

- a) The amendment to the definition of A^1 , where the first structure in line 1, page 4 of the amendment contains the variable B^1 where B^1 is NR^a and the variable R^{79} where R^{79} is OR^a is not defined in the specification with respect to the genus.
- b) The amendment to the definition of A^1 , where the first structure in line 2, page 4 of the amendment contains the variable R^{79} where R^{79} is OR^a or OH is not defined in the specification with respect to the genus.

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- c) The amendment to the definition of A^1 , where the second structure in line 2, page 4 of the amendment contains the variable B^2 where B^2 is CH is not defined in the specification with respect to the genus.
- d) The amendment to the definition of A^1 , where the second structure in line 3, page 4 of the amendment contains the variable R^{79} where R^{79} is OR^a or OH is not defined in the specification with respect to the genus.
- e) The amendment to the definition of A^1 , where the third structure in line 4, page 4 of the amendment contains the moiety imidazolin-2-ylamino, which is not defined in the specification with respect to the genus.
- f) The amendment to the definition of A^1 , where the fourth structure in line 4, page 4 of the amendment contains the moiety tetrahydropyrimidin-2-ylamion, which is not defined in the specification with respect to the genus.
- g) The amendment to the definition of A^1 , where the first structure in line 2, page 5 of the amendment contains the variable X^7 where X^7 is NR^a or CF_2 and the variable R^{79} where R^{79} is OR^a or OH is not defined in the specification with respect to the genus.
- h) The amendment to the definition of A^1 , where the first structure in line 3, page 5 of the amendment contains the variable X^8 where X^8 is CH_2 , NR^a and $CONR^a$ where R^a is alkyl or amino and the variable R^{79} where R^{79} is OR^a or OH is not defined in the specification with respect to the genus.
- i) The amendment to the definition of A^1 , where the second structure in line 3, page 5 of the amendment contains the variable B^7 where B^7 is NR^a ; the

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variable R^{81} where R^{81} is OR^a and where the aromatic ring is phenyl is not defined in the specification with respect to the genus.

Applicant is required to cancel the new matter in the reply to this Office action.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

6. Claims 8, 10, 11, 13 and 15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

- a) Claim 8 and claims dependent thereon are vague and indefinite in that it is not known what is meant by the definition of A1 where there is no variable A1 in formula I.
- b) Claim 8 and claims dependent thereon are vague and indefinite in that it is not known what is meant by the first moiety on page 5 of the amendment which fails to indicate the point of attachment.
- c) Claim 8 and claims dependent thereon are vague and indefinite in that it is not known what is meant by the definition of B^2 where B^2 is N and CH. B^2 is a divalent moiety in the second structure in line 2, page 4 of the amendment of which there is no substituent indicated and hence it is not known what else is attached to the N or CH group of B^2 .

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

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A person shall be entitled to a patent unless –


(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 8, 10, 11, 13 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by MILLER et al., WO 97/24119. Miller teaches the compounds, compositions and method of use of the compounds of the instant invention where X is $(\text{CHR}^p)_n$ where R^p is H and n is 1; the n of $(\text{CH}_2)_n$ is zero; R^b is OH; $A^1-Z^2-Z^1$ - is benzimidazol-2-ylmethylaminocarbonyl. See example 76.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda Coleman whose telephone number is 571-272-0665. The examiner can normally be reached on 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached on 571-272-0674. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Brenda Coleman
Primary Examiner Art Unit 1624
August 6, 2004